DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 18 January 2008 has been entered.

Status of the Claims

2. This action is in response to papers filed 18 January 2008 in which the previous rejections were traversed.

Applicant’s arguments have been thoroughly reviewed and are discussed below.

The previous rejections in the Office Action dated 27 September 2007 are maintained.

Claims 9-13 are under prosecution.

3. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Claim Objections

4. Claim 10 is objected to because of the following informalities: DNA is misspelled “DNS”. Appropriate correction is required.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meade (U.S. Patent No. 6,248,229, issued 19 June 2001) in view of Sorge (U.S. Patent No. 7,183,052, filed 17 July 2007) or Ullman et al (U.S. Patent Application Publication No. 2003/0152924, filed 7 December 2001).

Regarding Claims 9-10, Meade discloses a method of DNA detection comprising, immobilizing a binding ligand and hybridizing a binding partner labeled with an electrochemically active compound (Column 17, lines 26-40) and wherein the binding partner is complementary to the target DNA (Column 24, lines 30-41), adding the target to the binding partner-binding ligand to derive a competitive reaction between the binding ligand and the target and detecting amount and type of DNA by measuring a current change in the electrochemical signal before and after the competitive reaction (e.g. decreased signal, Column 24, lines 38-41) and wherein the detection is via a change in current (Columns 20-23, especially, Column 21, lines 25-43).

Meade specifically states that the target is detected following target competition for the binding partner (Column 24, lines 38-41). The favored hybridization and target detection of Meade would require favored complementation between the target and binding partner. Meade teaches the method wherein the binding partner is disassociated from the binding ligand, but does not specifically teach forming a double strand hybrid by applying heat to facilitate the dissociation of the binding partner and binding ligand followed by subsequent cooling.

However, heating and cooling to facilitated target detection during competitive hybridization between complementary probes was well known in the art at the time the claimed invention was made as taught by Ullman and Sorge.

Sorge teach a similar method of DNA detection comprising immobilizing complementary probe DNA and signaling DNA, adding a target DNA to derive a competitive reaction between the probe and target, heating near the melting temperature of the probe-signal hybrid and cooling to form a target-signal hybrid which is then detected (Column 4, lines 28-60; Column 10, lines 14-48; and Examples 2-4). Sorge further teach the probes are designed to dissociated under repeated heating and cooling conditions (e.g. PCR) to facilitate probe-target binding (Column 13, lines 50-Column 14, line 15, Examples 2-4).

Ullman also teach a similar method of DNA detection comprising providing complementary probe DNA and signaling DNA, adding a target DNA to derive a competitive reaction between the probe and target, heating near the melting temperature of the probe-signal hybrid and cooling to form a target-signal hybrid which is then detected (e.g. ¶ 105).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the heating and cooling cycles of Sorge and Ullman to the competitive hybridization of Meade. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success based on the well known, routinely practiced and preferred use of heating and cooling taught by Sorge and Ullman.

Regarding Claim 11, Meade discloses the method wherein the amount of target is quantified by measuring a change in signal before and after the competitive reaction (Column 21, lines 25-43).

Regarding Claim 12, Meade does not teach the probes correspond to several types of expected target sequence. However, Ullman teaches the similar method wherein the type of DNA is determined by a competitive reaction between a plurality of allele-specific probe DNA/signaling DNA hybrids and target and measuring a signal to identify the target (¶ 169-171) and Sorge teach the similar method wherein the type of DNA is determined by a competitive reaction between a plurality of allele-specific probe DNA/signaling DNA hybrids and target and measuring a signal to identify the target (Column 10, line 14-55).

Regarding Claim 13, Meade discloses the method wherein the DNA chip comprises at least two different probe DNAs, each fixed to an electrode of an electrode array (Column 17, lines 26-41).

Response to Arguments

7. Applicant traverses the rejection over Meade in view of Sorge or Ullman because Meade does not teach the complementarity of signal DNA and target DNA is higher than complementarity of probe DNA and signaling DNA. Applicant further asserts that, in this instance, it is proper to address only one of the cited references because "the test is what the combined teaching of the references would have suggested". Applicant's assertions are noted. It is further noted that it is the teaching of "the combined references" (note the plural form of references) that are relied upon in the rejection and In re Keller as cited. Furthermore, as stated in the office action, Meade specifically teaches a "competition assay" using probe, signal and target. While Meade does not specifically teach differences in complementation, the

reference does teach the binding ligand (probe) is "similar" to the target (Column 24, lines 37-39). Furthermore, the teaching of Sorge (cited in the previous office action) define competition assays using "target-like" probes, which have one or more mismatch compared to the target (Column 9, lines 39-Column 10, line 30). Hence, the combined teachings of the references obviate the instantly claimed invention.

8. Claims 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wohlstadter et al (U.S. Patent No. 6,207,369, issued 27 March 2001) in view of Hill et al (U.S. Patent No. 4,840,893, issued 20 June 1989), Sorge (U.S. Patent No. 7,183,052, filed 17 July 2007) and/or Ullman et al (U.S. Patent Application Publication No. 2003/0152924, filed 7 December 2001).

Regarding Claims 9-10, Wohlstadter et al disclose a method for detecting DNA comprising preparing a chip comprising probe DNA fixed to electrodes (Column 89, lines 42-45) wherein the probe DNA hybridizes to signaling DNA wherein probe DNA is also complementary to the target DNA and wherein the signaling DNA is labeled with an electrochemically active compound (i.e. ECL-TAG-a labeled sequences which can compete with the analytes of interest for binding surface immobilized probes, Column 89, lines 49-61), the method further comprises applying target DNA to the surface to derive a competitive reaction among the probe DNA, the signaling DNA and the target DNA and detecting amount and type of target DNA by detecting a change in electrochemical signal (Column 48, lines 13-48).

The comparative complementation recited in Claim 9 is deemed to be inherent in the competition assay of Wohlstadter because if hybridization between the target and binding partner is not favored, the binding partner would remain hybridized to the immobilized binding ligand and the assay would not function to detect the target. Wohlstadter specifically states that the target is detected following target competition for the binding partner (Column 24, lines 38-41). The favored hybridization and target detection of Wohlstadter would require a favored complementation between the target and binding partner.

Wohlstadter teaches that devices for measuring current are used in the method (Column 5, lines 27-34) but does not specifically teach that the changed electrochemical signal is via current measurement. However, current measurements to detect a target was well known in the art at the time the claimed invention was made as taught by Hill et al.

Hill et al teach a similar method for detecting a target comprising a probe + ligand, probe being complementary to the target, a second ligand + electrochemical label and an anti-ligand. The probe-ligand and second ligand are binding partners for the anti-ligand. In the presence of target, the probe-ligand is not available for binding to the anti-ligand, the electrochemically labeled second ligand binds the anti-ligand whereby current is measured to determine the presence of target (Column 2, lines 1-56). Hill et al teaches that the change is current is proportional to the amount of target present and the degree of homologous binding between the probe and target results in a measurable change in current (Column 7, lines 29-58). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the current detection of Hill et al to the target detection of Wohlstadter et al. One of ordinary skill in the art would have been motivated to do so based on the devices suggested by Wohlstadter (Column 5, lines 27-34). One would have been further motivated for the expected benefit of determining the amount of target and degree of homologous binding by simple measurement of current as taught by Hill et al (Column 7, lines 29-58). Wohlstadter et al does not teach repeated heating and cooling.

However, heating and cooling to facilitated target detection during competitive hybridization between complementary probes was well known in the art at the time the claimed invention was made as taught by Ullman and Sorge.

Sorge teach a similar method of DNA detection comprising immobilizing complementary probe DNA and signaling DNA, adding a target DNA to derive a competitive reaction between the probe and target, heating near the melting temperature of the probe-signal hybrid and cooling to form a target-signal hybrid which is then detected (Column 4, lines 28-60; Column 10, lines 14-48; and Examples 2-4). Sorge further teach the probes are designed to dissociated under repeated heating and cooling conditions (e.g. PCR) to facilitate probe-target binding (Column 13, lines 50-Column 14, line 15, Examples 2-4).

Ullman also teach a similar method of DNA detection comprising providing complementary probe DNA and signaling DNA, adding a target DNA to derive a competitive reaction between the probe and target, heating near the melting temperature of the probe-signal hybrid and cooling to form a target-signal hybrid which is then detected (e.g. ¶ 105).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the heating and cooling cycles of Sorge and Ullman to the competitive hybridization of Wohlstadter et al. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success based on the well known, routinely practiced and preferred use of heating and cooling taught by Sorge and Ullman.

Regarding Claim 11, Wohlstadter et al disclose the method wherein the amount of target DNA is quantified by measuring a change before and after the competitive reaction (Column 49, lines 19-22).

Regarding Claim 12, Wohlstadter et al disclose the method wherein the type of DNA is determined by a competitive reaction between double strands of probe DNA/signaling DNA and an unknown target and measuring a signal produced from the competitive reaction on an electrode array (Fig. 42, Example 6.35-6.37, Column 89, line 19-Column 91, line 20).

Regarding Claim 13, Wohlstadter et al disclose the method wherein multiple DNA detection is performed using the chip having double strands of probe DNA/signaling DNA to each electrode of an electrode array (Fig. 42, Example 6.35, Column 89, lines 19-62).

Response to Arguments

9. Applicant also traverses the rejection over Wohlstadter in view of Hill or Ullman because the method of Wohlsdatere requires additional steps. The argument is not sufficient to overcome the rejection because the open claim language "comprising" as recited in the instant claims encompassed the additional steps of the reference. Furthermore, there is no language in the instant claims that prohibits the additional step. Applicant traverse the citation of Hill for current measurement, stating that "why this is not disclosed in Wohlstadter if in fact the comparative complementation were to be inherent, as purported in the office action". The basis for this argument is unclear to the examiner. As stated in the office action, Wohlstadter teaches that devices for measuring current are used in the method (Column 5, lines 27-34) but does not specifically teach that the changed electrochemical signal is via current measurement. However, current measurements to detect a target were well known in the art at the time the claimed invention was made as taught by Hill et al. Hill et al teaches that the change is current is proportional to the amount of target present and the degree of homologous binding between the probe and target results in a measurable change in current (Column 7, lines 29-58). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the current detection of Hill et al to the target detection of Wohlstadter et al. One of ordinary skill in the art would have been motivated to do so based on the devices suggested by Wohlstadter (Column 5, lines 27-34). One would have been further motivated for the expected benefit of determining the amount of target and degree of homologous binding by simple measurement of current as taught by Hill et al (Column 7, lines 29-58). Applicant has not addressed the motivation provided. In contrast to addressing the arguments, Applicant merely asks why one would combine the teachings. The examiner can only respond by referring to the reasoning provided in the office action, which are not addressed by or proved wrong by Applicant.

Conclusion

10. No claim is allowed.
11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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